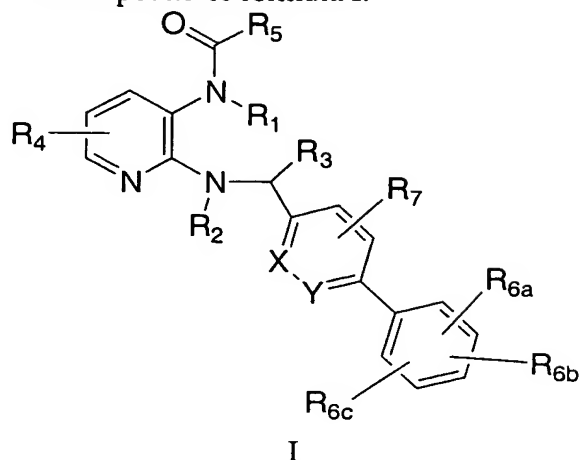


## WHAT IS CLAIMED IS:

1. A compound of formula I:



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wherein

X and Y are each CH, or one is CH and the other is N;

R<sub>1</sub> and R<sub>2</sub> are independently selected from

- (1) hydrogen and  
 (2) C<sub>1-4</sub> alkyl;

10

R<sub>3</sub> is selected from

- (1) hydrogen, and  
 (2) C<sub>1-4</sub> alkyl optionally substituted with 1 to 4 groups selected from halogen, CO<sub>2</sub>R<sup>a</sup>, OR<sup>a</sup>, COR<sup>a</sup> and cyano;

15 R<sub>4</sub> is selected from

- (1) hydrogen,  
 (2) nitro,  
 (3) halogen,  
 (4) (CH<sub>2</sub>)<sub>n</sub>OR<sup>a</sup>,  
 (5) (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R<sup>a</sup>,  
 (6) (CH<sub>2</sub>)<sub>n</sub>CN,  
 (7) (CH<sub>2</sub>)<sub>n</sub>NR<sup>b</sup>R<sup>c</sup>,  
 (8) (CH<sub>2</sub>)<sub>n</sub>NHC(O)CH<sub>2</sub>CN,  
 (9) CONR<sup>b</sup>R<sup>c</sup>, and  
 (10) C<sub>1-4</sub> alkyl;

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R<sub>5</sub> is selected from

- (1) C<sub>1-6</sub>alkyl,
- (2) methyl substituted with C<sub>3-6</sub>cycloalkyl, CO<sub>2</sub>R<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>,  
CONR<sup>b</sup>R<sup>c</sup>, OR<sup>a</sup>, NR<sup>b</sup>R<sup>c</sup>, NO<sub>2</sub>, N<sub>3</sub> or aryl,
- (3) C<sub>3-6</sub>cycloalkyl,
- 5 (4) C<sub>2-6</sub>alkenyl,
- (5) CONR<sup>b</sup>R<sup>c</sup>,
- (6) OR<sup>a'</sup>, wherein R<sup>a'</sup> is a non-hydrogen group selected from R<sup>a</sup>,
- (7) COR<sup>a</sup>, and
- (8) NR<sup>b</sup>R<sup>c</sup>;
- 10 with the proviso that when R<sub>5</sub> is n-propyl, n-butyl or cyclopropyl, R<sub>4</sub> is 4-methyl, and  
R<sub>6b</sub> and R<sub>6c</sub> are each H, then R<sub>6a</sub> is not 2-(4,4-dimethyl-4,5-dihydro-1,3-oxazole), 2-  
CN or 2-CO<sub>2</sub>Me;  
R<sub>6a</sub> is selected from
- (1) C<sub>1-8</sub> alkyl, optionally substituted with 1 to 5 groups
- 15 independently selected from halogen, nitro, cyano, COR<sup>a</sup>, SO<sub>2</sub>R<sup>d</sup>, CO<sub>2</sub>R<sup>a</sup>, NR<sup>b</sup>R<sup>c</sup>,  
NR<sup>b</sup>C(O)R<sup>a</sup>, NHSO<sub>2</sub>R<sup>d</sup>, OR<sup>a</sup>, OC(O)R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>,
- (2) C<sub>3-8</sub> cycloalkyl,
- (3) C<sub>2-8</sub> alkenyl optionally substituted with CO<sub>2</sub>R<sup>a</sup>;
- (4) halogen,
- 20 (5) OCF<sub>3</sub>,
- (6) cyano,
- (7) nitro,
- (8) NR<sup>b</sup>R<sup>c</sup>,
- (9) NR<sup>b</sup>C(O)R<sup>a</sup>,
- 25 (10) NR<sup>b</sup>CO<sub>2</sub>R<sup>a'</sup>, wherein R<sup>a'</sup> is a non-hydrogen group selected  
from R<sup>a</sup>,
- (11) CO<sub>2</sub>R<sup>a</sup>,
- (12) COR<sup>a</sup>,
- (13) C(O)NR<sup>b</sup>R<sup>c</sup>,
- 30 (14) C(O)NHO<sup>a</sup>,
- (15) OR<sup>a</sup>,
- (16) OC(O)R<sup>a</sup>,
- (17) S(O)<sub>n</sub>R<sup>a'</sup>, wherein R<sup>a'</sup> is a non-hydrogen group selected from  
R<sup>a</sup>,

- (18)  $\text{SO}_2\text{NHR}^c$ ,  
 (19)  $\text{NHSO}_2\text{R}^d$ ,  
 (20)  $\text{C}(=\text{NOR}^a)\text{NR}^b\text{R}^c$ ,  
 (21)  $\text{C}(=\text{NOR}^a)\text{R}^a$ , and  
 5 (22) substituted or unsubstituted heterocycle where the heterocycle is selected from oxadiazole, tetrazole, triazole, pyrazole, oxazole, isoxazole, thiazole, 4,5-dihydro-oxazole, 4,5-dihydro-1,2,4-oxadiazol-5-one, and wherein said substituent is 1 to 3 groups independently selected from  $\text{C}_{1-4}$ alkyl optionally substituted with 1 to 5 halogen atoms,  $\text{OR}^a$ , or  $\text{OC}(\text{O})\text{R}^a$ ;  
 10  $\text{R}_{6b}$  and  $\text{R}_{6c}$  are independently selected from  
 (1) hydrogen, and  
 (2) a group from  $\text{R}_{6a}$ ; with the proviso that not more than one of  $\text{R}_{6a}$ ,  $\text{R}_{6b}$ , and  $\text{R}_{6c}$  is a heterocycle;  
 $\text{R}_7$  is selected from  
 15 (1) hydrogen,  
 (2) cyano,  
 (3) nitro,  
 (4) halogen,  
 (5)  $\text{OR}^a$ ,  
 20 (6)  $\text{CO}_2\text{R}^a$ ,  
 (7)  $\text{CONR}^b\text{R}^c$ , and  
 (8)  $\text{C}_{1-4}$  alkyl;  
 $\text{R}^a$  is selected from  
 25 (1) hydrogen,  
 (2)  $\text{C}_{1-4}$  alkyl,  
 (3)  $\text{C}_{3-6}$  cycloalkyl,  
 (4) aryl, and  
 (5) aryl- $\text{C}_{1-4}$  alkyl;  
 $\text{R}^b$  and  $\text{R}^c$  are independently selected from  
 30 (1) hydrogen,  
 (2)  $\text{C}_{1-4}$  alkyl optionally substituted with  $\text{OR}^a$ ,  
 (3)  $\text{C}_{3-6}$  cycloalkyl,  
 (4) aryl, and  
 (5) aryl- $\text{C}_{1-4}$  alkyl; or

R<sup>b</sup> and R<sup>c</sup> together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally containing a heteroatom selected from NR<sup>a</sup>, O and S;

R<sup>d</sup> is selected from

- (1) C<sub>1-4</sub> alkyl, optionally substituted with 1 to 3 halogen atoms,
- (2) aryl,
- (3) aryl-C<sub>1-4</sub> alkyl, and
- (4) NR<sup>b</sup>R<sup>c</sup>;

n is 0, 1 or 2

a pharmaceutically acceptable salt thereof.

10

2. A compound of Claim 1 wherein R<sub>3</sub> is hydrogen.

3. A compound of Claim 1 wherein R<sub>3</sub> is C<sub>1-4</sub> alkyl.

15

4. A compound of Claim 1 wherein R<sub>4</sub> is H or a 4-substituent.

5. A compound of Claim 1 wherein R<sub>4</sub> is H or a 4-substituent selected from C<sub>1-4</sub> alkyl and halogen.

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6. A compound of Claim 1 wherein R<sub>4</sub> is 4-chloro or 4-methyl.

7. A compound of Claim 1 wherein R<sub>5</sub> is selected from ethyl, n-propyl, isopropyl, n-butyl, isobutyl, cyclopropyl and cyclopentylmethyl.

25

8. A compound of Claim 1 wherein R<sub>5</sub> is selected from C<sub>3-6</sub>alkenyl and methyl substituted with CO<sub>2</sub>R<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>, OR<sup>a</sup>, NR<sup>b</sup>R<sup>c</sup>, N<sub>3</sub>.

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9. A compound of Claim 1 wherein X and Y are both CH.

10. A compound of Claim 1 wherein one of X and Y is CH and the other is N.

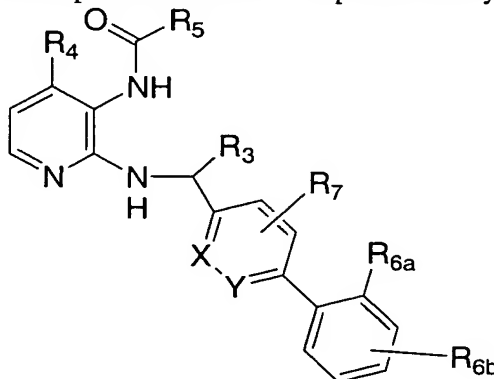
11. A compound of Claim 1 wherein  $R_{6a}$  is a 2- (or ortho-) substituent selected from  $CO_2R^a$ ,  $CONR^bR^c$ ,  $CONHOR^a$ ,  $C_{1-8}$  alkyl substituted with 1 to 5 halogen atoms, cyano,  $SO_2NHR^c$ , and 1,2,4-oxadiazolyl optionally substituted with  $C_{1-4}$ alkyl optionally substituted with 1-5 halogen atoms,  $OR^a$  or  $OC(O)R^a$ .

12. A compound of Claim 11 wherein  $R_{6a}$  is selected from 1,2,4-oxadiazolyl optionally substituted with  $C_{1-4}$ alkyl optionally substituted with 1-5 halogen atoms,  $OR^a$  or  $OC(O)R^a$ .

13. A compound of Claim 1 wherein  $R_{6b}$  is selected from hydrogen,  $C_{1-8}$  alkyl optionally substituted with OH or 1 to 5 halogen atoms,  $NR^bR^c$ ,  $OR^a$ , and nitro, and  $R_{6c}$  is hydrogen.

14. A compound of Claim 13 wherein  $R_{6b}$  is hydrogen, amino, nitro, methyl carboxylate, chloro, or methyl.

15. A compound of Claim 1 represented by formula Ia:



Ia

wherein  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_{6a}$ ,  $R_{6b}$ ,  $R_7$ , X and Y are as defined in Claim 1.

16. A compound of Claim 15 wherein at least one of  $R_3$ ,  $R_4$  and  $R_{6b}$  is non-hydrogen.

17. A compound of Claim 15 wherein at least two of  $R_3$ ,  $R_4$  and  $R_{6b}$  are non-hydrogen.

18. A compound of Claim 15 wherein R<sub>6a</sub> is selected from CO<sub>2</sub>R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>, CONHOR<sup>a</sup>, C<sub>1-8</sub> alkyl substituted with 1 to 5 halogen atoms, cyano, SO<sub>2</sub>NHR<sup>c</sup>, 1,2,4-oxadiazolyl optionally substituted with C<sub>1-4</sub>alkyl optionally substituted with 1-5 halogen atoms, OR<sup>a</sup> or OC(O)R<sup>a</sup>.

19. A compound of Claim 18 wherein R<sub>6a</sub> is selected from 1,2,4-oxadiazolyl optionally substituted with C<sub>1-4</sub>alkyl optionally substituted with 1-5 halogen atoms, OR<sup>a</sup> or OC(O)R<sup>a</sup>.

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20. A compound of Claim 19 wherein R<sub>6b</sub> is hydrogen.

21. A compound of Claim 15 wherein R<sub>5</sub> is n-propyl.

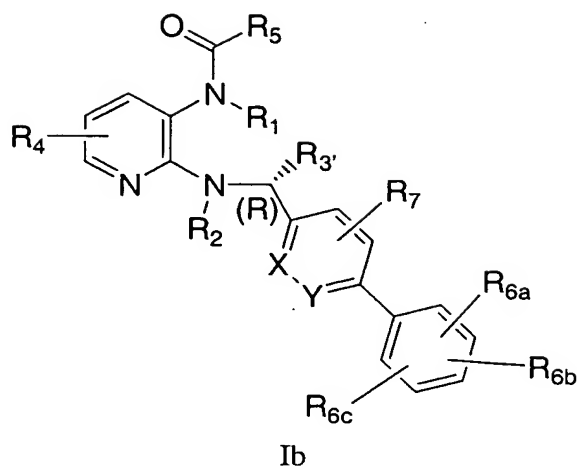
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22. A compound of Claim 15 wherein R<sub>5</sub> is selected from methyl substituted with CO<sub>2</sub>R<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>.

23. A compound of Claim 15 wherein  
 R<sub>3</sub> is H or C<sub>1-4</sub> alkyl;  
 R<sub>4</sub> is H, C<sub>1-4</sub> alkyl or halogen;  
 R<sub>5</sub> is R<sub>5</sub> is selected from ethyl, n-propyl, isopropyl, n-butyl, isobutyl, cyclopropyl, cyclopentylmethyl, C<sub>3-6</sub>alkenyl and methyl substituted with CO<sub>2</sub>R<sup>a</sup>, SO<sub>2</sub>R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>, OR<sup>a</sup>, NR<sup>b</sup>R<sup>c</sup>, N<sub>3</sub>;  
 R<sub>6a</sub> CO<sub>2</sub>R<sup>a</sup>, CONR<sup>b</sup>R<sup>c</sup>, CONHOR<sup>a</sup>, C<sub>1-8</sub> alkyl substituted with 1 to 5 halogen atoms, cyano, SO<sub>2</sub>NHR<sup>c</sup>, 1,2,4-oxadiazolyl optionally substituted with C<sub>1-4</sub>alkyl optionally substituted with 1-5 halogen atoms, OR<sup>a</sup> or OC(O)R<sup>a</sup>;  
 R<sub>6b</sub> hydrogen; and  
 R<sub>6c</sub> is hydrogen; with the proviso that at least one of R<sub>3</sub>, R<sub>4</sub> and R<sub>6b</sub> is nonhydrogen.

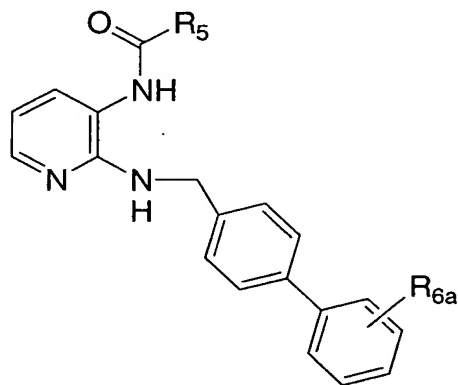
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24. A compound of Claim 1 represented by the formula Ib:



- wherein all the variables are as defined in Claim 1, except R<sub>3'</sub> is C<sub>1-4</sub> alkyl optionally substituted with 1 to 4 groups selected from halogen, CO<sub>2</sub>R<sup>a</sup>, OR<sup>a</sup>, COR<sup>a</sup> and cyano.

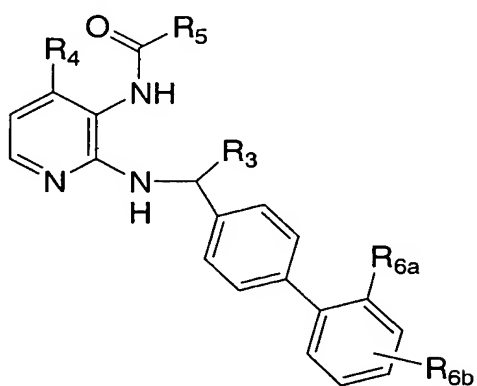
25. A compound selected from:



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R <sub>6a</sub>	R <sub>5</sub>
3'-CHO	nBu
4'-CH <sub>2</sub> OH	nBu
3'-CN	nBu
5'-CN	nBu
4'-CHO	nBu

R <sub>6a</sub>	R <sub>5</sub>
3'-COMe	nBu
4'-COMe	nBu
3'-CH <sub>2</sub> OH	nBu
3'-CH(OH)CH <sub>3</sub>	nBu
4'-CH(OH)CH <sub>3</sub>	nBu
4'-CO <sub>2</sub> Me	nPr
3'-CO <sub>2</sub> Me	nPr
3'-NH <sub>2</sub>	nBu
4'-OMe	nPr
4'-Cl	nPr
3'-OCH <sub>3</sub>	nBu
4'-CF <sub>3</sub>	nBu
4'-OCF <sub>3</sub>	nBu
4'-OEt	nBu
4'-NO <sub>2</sub>	nBu
4'-SMe	nBu
3'-NO <sub>2</sub>	nBu



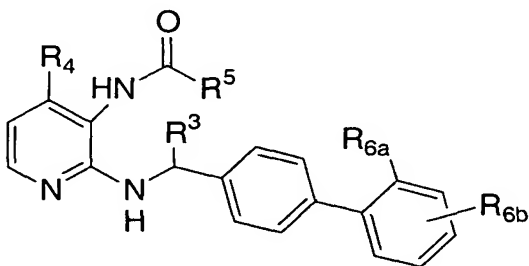
R <sub>6a</sub>	R <sub>6b</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
CO <sub>2</sub> Me	5'-Me	Me(R)	Me	n-Pr
CO <sub>2</sub> Me	6'-Me	Me(R)	Me	nPr



R6a	R6b	R3	R4	R5
3-Me-1,2,4-oxadiazol-5-yl	H	H	H	nPr
CONHOMe	H	H	H	nPr
5-Me-1,2,4-oxadiazol-3-yl	H	H	H	nPr
5-(CH <sub>2</sub> OH)-1,2,4-oxadiazol-3-yl	H	H	H	nPr
3-(acetoxymethyl)-1,2,4-oxadiazolyl	H	H	H	nPr
CO <sub>2</sub> Me	H	H	H	nPr
CO <sub>2</sub> Et	H	H	H	nPr
SO <sub>2</sub> NHCH <sub>3</sub>	H	H	H	nPr
CF <sub>3</sub>	H	Me	H	nPr
CO <sub>2</sub> Me	6'-NH <sub>2</sub>	H	H	nPr
1 and 2-Me-tetrazol-5-yl (mixture)	H	H	H	nPr
CO <sub>2</sub> Me	H	H	H	Et
5-(CH <sub>2</sub> F)-1,2,4-oxadiazol-3-yl	H	H	H	nPr
1,3,4-oxadiazol-2-yl	H	H	H	nPr
CO <sub>2</sub> Me	H	H	H	iBu
4,5-dihydro-2-oxazolyl	H	H	H	nPr
NHCO <sub>2</sub> Me	H	H	H	nPr
CH <sub>2</sub> CN	H	H	H	nPr
CH <sub>2</sub> NHSO <sub>2</sub> Me	H	H	H	nPr
CO <sub>2</sub> Me	H	H	H	cPr
CO <sub>2</sub> Me	4'-CO <sub>2</sub> Me	H	H	nPr
CO <sub>2</sub> Me	H	H	H	n-Bu
2-oxazolyl	H	H	H	nPr
CF <sub>3</sub>	H	H	H	nPr
CO <sub>2</sub> Me	H	H	H	i-Pr
1N-tetrazole	H	H	H	nPr
NO <sub>2</sub>	H	H	H	nPr
CHO	H	H	H	nPr
5-Me-1,3,4-oxadiazol-2-yl	H	H	H	nPr
3-(methyl (2E)-3-prop-2-enoate)	H	H	H	nBu
CO <sub>2</sub> Me	H	H	H	CH <sub>2</sub> -cPen

R <sub>6a</sub>	R <sub>6b</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
CN	H	H	H	nPr
CONHCH <sub>3</sub>	H	H	H	nBu
CO <sub>2</sub> -cPen	H	H	H	nPr
CH <sub>2</sub> NHSO <sub>2</sub> Et	H	H	H	nPr
SO <sub>2</sub> NHtBu	H	Me	H	nPr
CH <sub>2</sub> CO <sub>2</sub> Me	H	H	H	nPr
CHO	H	H	H	n-Bu
NHAc	H	H	H	nPr
Cl	H	H	H	nPr
CO <sub>2</sub> Me	6'-NO <sub>2</sub>	H	H	nPr
5-Me-4,5-dihydro-2-oxazolyl	H	H	H	nPr
COMe	H	H	H	nPr
Me 3-propanoate	H	H	H	nBu
CO <sub>2</sub> Me	4'-Cl	H	H	nPr
SO <sub>2</sub> NH-t-Bu	H	H	H	nPr
C(=NOH)Me	H	H	H	nBu
CONH(CH <sub>2</sub> ) <sub>2</sub> OH	H	H	H	nPr
CH <sub>2</sub> NHSO <sub>2</sub> N(Me) <sub>2</sub>	H	H	H	nPr
CH <sub>3</sub>	H	H	H	nPr
COMe	H	H	H	nBu
CONH <sub>2</sub>	H	H	H	nBu
CH(OH)CH <sub>3</sub>	H	H	H	nBu
CH <sub>2</sub> OH	H	H	H	nBu
OEt	H	H	H	nBu
NH <sub>2</sub>	H	H	H	nPr
CH <sub>2</sub> NH <sub>2</sub>	H	H	H	nPr
OMe	H	H	H	nBu
SMe	H	H	H	nPr
C(=NOH)NH <sub>2</sub>	H	H	H	nPr
1H-tetrazol-5-yl	H	H	H	nPr
CH <sub>2</sub> NHAc	H	H	H	nPr

R <sub>6a</sub>	R <sub>6b</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
CO <sub>2</sub> Me	4'-NH <sub>2</sub>	H	H	nPr
OMe	5'-OMe	H	H	nBu
SO <sub>2</sub> Me	H	H	H	nPr
4-Me-4,5-dihydro-2-oxazolyl	H	H	H	nPr
Cf(=NOMe)Me	H	H	H	nBu
CO <sub>2</sub> Me	4'-OMe	H	H	nPr
4,4-dimethyl-4,5-dihydro-2-oxazolyl)	H	H	H	nPr
CH <sub>2</sub> NHC(O)-cPr	H	H	H	nPr
4-Me-2-thiazolyl	H	H	H	nPr
4-Me-2-thiazolyl	H	H	H	nPr
CONHCH(OH)CH <sub>2</sub> OH	H	H	H	nPr
CONHCH <sub>2</sub> CH(OH)CH <sub>3</sub>	H	H	H	nPr
CO <sub>2</sub> Me	4'-CO <sub>2</sub> H	H	H	nPr
CO <sub>2</sub> Me	4'-NO <sub>2</sub>	H	H	nPr
4,5-dimethyl-2-thiazolyl	H	H	H	nPr
4,5-dimethyl-2-thiazolyl	H	H	H	nPr
2-OH-1,1-dimethylethanecarboxamide	H	H	H	nPr



R <sub>6a</sub>	R <sub>6b</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
CO <sub>2</sub> Me	3'-F	Me (R)	Cl	CH <sub>2</sub> CO <sub>2</sub> Me
CO <sub>2</sub> Me	5'-Me	Me (R)	Me	CH <sub>2</sub> SO <sub>2</sub> Me
SO <sub>2</sub> NHMe	H	Me (R)	Me	CH <sub>2</sub> CONH <sub>2</sub>
CO <sub>2</sub> Me	H	H	H	CH <sub>2</sub> SO <sub>2</sub> Me

R <sub>6a</sub>	R <sub>6b</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>
CO <sub>2</sub> Me	H	H	Me	(E)-propenyl
CO <sub>2</sub> Me	H	H	Me	CH <sub>2</sub> N <sub>3</sub>
CO <sub>2</sub> Me	H	H	H	CH <sub>2</sub> OCH <sub>3</sub>
CO <sub>2</sub> Me	H	H	H	CONH <sub>2</sub>
CO <sub>2</sub> Me	H	H	H	CH <sub>2</sub> NMe <sub>2</sub>
CO <sub>2</sub> Me	H	H	H	OEt
CO <sub>2</sub> Me	H	H	H	benzyl
CO <sub>2</sub> Me	H	H	H	CH <sub>2</sub> NO <sub>2</sub>
CO <sub>2</sub> Me	H	H	H	COPh
CO <sub>2</sub> Me	H	H	Me	NHEt

26. A pharmaceutical composition comprising a compound according to Claim 1 or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

5

27. A method of treatment or prevention of pain and inflammation comprising a step of administering, to a subject in need of such treatment or prevention, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

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28. A method of treatment of osteoarthritis, repetitive motion pain, dental pain, cancer pain, myofascial pain, muscular injury pain, fibromyalgia pain, perioperative pain comprising a step of administering, to a subject in need of such treatment, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

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29. A method of treatment or prevention of inflammatory pain caused by chronic obstructive pulmonary disease, asthma, inflammatory bowel disease, rhinitis, pancreatitis, cystitis (interstitial cystitis), uveitis, inflammatory skin disorders, rheumatoid arthritis, edema resulting from trauma associated with burns, sprains or fracture, postsurgical intervention, osteoarthritis, rheumatic disease, teno-synovitis, or gout comprising a step of administering, to a subject in need of such treatment or

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prevention, an effective amount of a compound according to Claim 1 or a pharmaceutically acceptable salt thereof.

5                   30. A method of treatment or prevention of pain associated with  
angina, menstruation or cancer comprising a step of administering, to a subject in  
need of such treatment or prevention, an effective amount of a compound according to  
Claim 1 or a pharmaceutically acceptable salt thereof.

10                   31. A method of treatment of diabetic vasculopathy, post capillary  
resistance, diabetic symptoms associated with insulinitis, psoriasis, eczema, spasms of  
the gastrointestinal tract or uterus, Crohn's disease, ulcerative colitis, or pancreatitis  
comprising a step of administering, to a subject in need of such treatment, an effective  
amount of a compound according to Claim 1 or a pharmaceutically acceptable salt  
thereof.

15                   32. A method of treatment or prevention of pain caused by  
pneumoconiosis, including aluminosis, anthracosis, asbestosis, chalicosis, ptilosis,  
siderosis, silicosis, tabacosis, byssinosis, adult respiratory distress syndrome,  
bronchitis, allergic rhinitis, vasomotor rhinitis, liver disease, multiple sclerosis,  
20   atherosclerosis, Alzheimer's disease, septic shock, cerebral edema, headache,  
migraine, closed head trauma, irritable bowel syndrome, or nephritis comprising a  
step of administering, to a subject in need of such treatment or prevention of pain, an  
effective amount of a compound according to Claim 1 or a pharmaceutically  
acceptable salt thereof.